Attorney's Docket No.: 06275-0492US1 / 101170-1P US

Applicant : Ambrose et al. Serial No. : 10/566,054 Filed : June 27, 2006 Page : 3 of 13

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

- 1. (Currently amended) A method of diagnosis comprising:
- (a) providing a biological sample from a human identified as being in need of treatment with a therapeutic agent that is transported by OATP-C rosuvastatin, wherein the sample comprises a nucleic acid encoding OATP-C;
 - (b) testing the nucleic acid for the presence, on at least one allele, of either
- (i) a codon encoding alanine at the position corresponding to position 174 of SEQ ID NO:1, or
 - (ii) an allele of a polymorphism in linkage disequilibrium with (i); and
- (c) if either (i) or (ii) is found in at least one allele, diagnosing the human as likely to have reduced ability to transport the therapeutic agent rosuvastatin into liver cells.
- (Withdrawn) A method according to claim 1 wherein the polymorphism of (b)(ii) is -26A>G, -118A>C, -309T>C, -878A>G, -903C>T, -1054G>T, -1215T>A, or -1558T>C, all of SEQ ID NO:2; or T2122G, C2158T, A2525C, or G2651A, all of SEQ ID NO:3.
- (Withdrawn) A method according to claim 1 wherein the polymorphism of (b)(ii) is selected from -118A>C and -1558T>C of SEQ ID NO:2.
- 4. (Currently amended) A method according to claim 1, wherein the therapeutic agent is a statin, the human is being treated with one dose level of <u>rosuva</u>statin and step (c) further comprises diagnosing the human as suitable for titration to another higher <u>rosuva</u>statin dose level

Attorney's Docket No.: 06275-0492US1 / 101170-1P

Applicant: Ambrose et al. Serial No.: 10/566,054 Filed: June 27, 2006

Page : 4 of 13

comprising monitoring for a decrease in benefit risk ratio resulting from the reduced ability to transport the statin into cells if cither (i) or (ii) is found in at least one allele.

- 5. 6. (Canceled)
- (Currently amended) A method according to claim [[5]] 1 wherein the human is being treated with at least 5 mg of [[a]] rosuvastatin daily.
- (Currently amended) A method according to claim [[5]] 1 wherein the human is being treated with at least 10 mg of [[a]] rosuvastatin daily.
- (Currently amended) A method according to claim [[5]] 1 wherein the human is being treated with at least 20 mg of [[a]] rosuvastatin daily.
- (Currently amended) A method according to claim [[5]] \(\frac{1}{2}\) wherein the human is being treated with at least 40 mg of [[a]] rosuvastatin daily.
- 11. (Currently amended) A method of diagnosis comprising:
- (a) providing a biological sample from a human identified as being in need of treatment with a therapeutic agent that is transported into cells by OATP C rosuvastatin, wherein the sample comprises an OATP-C polypeptide;
- (b) determining whether the amino acid of the OATP-C polypeptide corresponding to position 174 of SEQ ID NO:1 is a valine; and
- (c) if the amino acid is not a valine, diagnosing the human as likely to have a reduced ability to transport the therapeutic agent rosuvastatin into liver cells.
- (Currently amended) A method according to claim 11, wherein the therapeutic agent is a statin, the human is being treated with one dose level of rosuvastatin and step (c) further

Attorney's Docket No.: 06275-0492US1 / 101170-1P US

Applicant: Ambrose et al. Serial No.: 10/566,054 Filed : June 27, 2006

: 5 of 13 Page

comprises diagnosing the human as suitable for titration to another, higher rosuvastatin dose level comprising monitoring for a decrease in benefit risk ratio resulting from the reduced ability to transport the statin into cells if the amino acid is not a valine.

- (Withdrawn-Currently amended) A method according to claim [[12]] 11, the method 13. further comprising measurement of measuring the level of OATP-C polypeptide expression with valine and/or alanine at position 174 whereby to determine the presence or absence of -118A>C polymorphism in OATP-C nucleic acid.
- 14. (Withdrawn-Currently amended) A method according to claim [[12]] 11, the method further comprising measuring OATP-C polymentide for presence or absence of OATP-C *15 allele whereby to determine the presence or absence of -118A>C polymorphism in OATP-C nucleic acid determining, in a sample of nucleic acid from the human, the presence or absence, on at least one allele, of a cytosine at the position corresponding to -118 of SEO ID NO:2, wherein the presence of the cytosine, combined with the determination that the amino acid of (b) is not a valine, is a further indication that the human is likely to have reduced ability to transport rosuvastatin into liver cells.
- 15 (Currently amended) A method according to claim [[12]] 11, wherein the amino acid at position 174 is determined to be alanine.
- 16. 17.(Canceled)
- (Currently amended) A method according to claim [[16]] 11, wherein the human is being 18 treated with at least 5 mg of [[all rosuvastatin daily.
- 19. (Currently amended) A method according to claim [[16]] 11, wherein the human is being treated with at least 10 mg of [[a]] rosuvastatin daily.

Applicant : Ambrose et al. Attorney's Docket No.: 06275-0492US1 / 101170-IP

Serial No.: 10/566,054 Filed: June 27, 2006 Page: 6 of 13

20. (Currently amended) A method according to claim [[16]] 11, wherein the human is being treated with at least 20 mg of [[a]] rosuvastatin daily.

- 21. (Currently amended) A method according to claim [[16]] 11, wherein the human is being treated with at least 40 mg of [[a]] rosuvastatin daily.
- 22. (New) A method according to claim 1, wherein the nucleic acid is tested both for the presence, on at least one allele, of a codon encoding alanine at the position corresponding to position 174 of SEQ ID NO:1 and for the presence, on at least one allele, of a cytosine at the position corresponding to position -118 of SEQ ID NO:2.